

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (Currently Amended) A double-stranded RNA complex comprising:
  - (a) a first portion comprising a first ribonucleic acid ~~molecule~~sequence capable of hybridizing under physiological conditions to at least a portion of an mRNA molecule; and
  - (b) a second portion comprising a second ribonucleic acid ~~molecule~~sequence, wherein at least a portion of ~~the second ribonucleic acid molecule~~which is capable of hybridizing under physiological conditions to the first portion.
2. (Currently Amended) ~~A~~The double-stranded RNA complex of claim 1 wherein the first and second portions are separate ribonucleic acid molecules.
3. (Currently Amended) ~~A~~The double-stranded RNA ~~molecule~~complex of claim 1 wherein the mRNA is ~~encoded by~~ transcribed from a gene in a cell.
4. (Currently Amended) A linear RNA molecule capable of forming a ~~dsRNA~~double-stranded RNA complex wherein the RNA molecule comprises:
  - (a) a first portion that hybridizes to at least a portion of an mRNA molecule; and
  - (b) a second portion wherein at least part of the second portion is capable of hybridizing to the first portion to form a hairpin ~~dsRNA~~double-stranded RNA complex.
5. (Currently Amended) ~~A~~The ~~double-stranded~~linear RNA molecule of claim 4 wherein the mRNA is ~~encoded by~~ transcribed from a gene in a cell.
6. (Currently Amended) ~~A~~The linear RNA molecule of claim 4 further comprising a third portion of ribonucleic acid ~~interposed~~ located between the first and second portions.

7. (Currently Amended) ~~A~~The linear RNA molecule of claim 6 wherein the third portion promotes hybridization between the first and second ~~portion~~portions.

8. (Currently Amended) ~~A~~The RNA molecule of ~~claims 1 or 4~~ claim 5 further comprising an additional ~~RNA~~ portion of ribonucleic acid that enhances the ability of ~~dsRNA~~double-stranded RNA to alter transcription from the gene ~~encoding~~ comprising the sequence of the mRNA molecule.

9. (Currently Amended) ~~A~~The RNA molecule of claim 8 wherein the additional RNA-portion ~~encodes an RNA molecule~~ comprises the sequence of an mRNA.

10. (Currently Amended) ~~A~~The RNA molecule of claim 8 wherein the additional RNA portion encodes a protein.

11. (Currently Amended) ~~A~~The RNA molecule of claim 10 wherein the protein is HIV Tat.

12. (Currently Amended) ~~A~~The RNA molecule of claim 6 wherein the third portion ~~of ribonucleic acid~~ further comprises at least one ribozyme and a target sequence recognizable by the ribozyme wherein the target sequence is not present in the first ~~portion~~ and the or second portionportions.

13. (Currently Amended) ~~A~~The RNA molecule of claim 12 wherein the double-stranded RNA complex is formed upon hybridization of the first and second ~~portion~~portions, and cleavage of the target sequence is ~~cleaved~~ mediated by the hairpin double-stranded RNA~~dsRNA~~.

14. (Currently Amended) ~~A~~The RNA molecule of claim 6 wherein the third portion ~~of ribonucleic acid~~ further comprises an intron or a linker sequence.

15. (Currently Amended) A linear RNA molecule capable of forming a double-stranded RNA~~dsRNA~~ complex wherein the RNA molecule comprises:

- (a) a first portion that comprises a region of RNA that is complementary to at least a portion of ~~aan~~ mRNA molecule ~~encoded by~~transcribed from a gene;
- (b) a second portion capable of hybridizing to at least part of the first portion; and
- (c) a third portion ~~positioned~~located between the first and second portions; said third portion promoting hybridization between ~~to permit~~ the first and second portions ~~to hybridize with one another.~~

16. (Currently Amended) ~~A~~The linear RNA molecule of claim 15 wherein the third portion comprises at least one ribozyme and a target sequence recognized by the ribozyme, wherein the target sequence is not present in the first or second ~~portion~~portions.

17. (Currently Amended) ~~A~~The linear RNA molecule of claim 15 wherein the ~~second sequence~~ portion comprises a polyadenylation signal.

18. (Currently Amended) ~~A~~The linear RNA molecule of claim 15 wherein the third portion ~~comprises~~comprises a plurality of ribozymes and target sequences capable of cleavage thereby.

19. (Currently Amended) A linear RNA molecule capable of forming a double-stranded RNA~~dsRNA~~ complex wherein the RNA molecule comprises:

- (a) a first portion that hybridizes to at least a portion of aan mRNA molecule ~~encoded by~~transcribed from a gene; and
- (b) a second portion wherein at least part of the second portion is capable of hybridizing to the first portion, and further wherein the second portion comprises a polyadenylation signal and a ribozyme positioned between the part of the second portion capable of hybridizing to the first portion and the polyadenylation signal, wherein the ribozyme is capable of removing the polyadenylation signal.

20. (Currently Amended) ~~A~~The linear RNA molecule of claim 19 wherein the ribozyme is a cis-acting hammerhead ribozyme.

21. (Currently Amended) ~~At least one~~A DNA molecule ~~encoding from which~~ the RNA ~~molecules~~molecule of ~~any of claims 1-20~~claim 12 can be transcribed.

22. (Currently Amended) A DNA molecule ~~of claim 21 wherein a single DNA molecule encodes from which~~ the RNA ~~molecules~~molecule of ~~any one of claims 1-20~~ claim 15 can be transcribed.

23. (Currently Amended) ~~A DNA molecule of claim 21 wherein two~~ One or more DNA molecules ~~encode from which~~ the double-stranded RNA ~~molecules~~ of claim 1 can be transcribed.

24. (Currently Amended) A eukaryotic cell comprising the RNA ~~molecules~~molecule of ~~claims 1-20~~claim 12.

25. (Currently Amended) A eukaryotic cell comprising the DNA of ~~molecules~~molecule of ~~any of claims 21-23~~claim 21.

26. (Currently Amended) ~~A~~The eukaryotic cell of ~~claims~~claim 24 or 25 wherein the cell is a mammalian cell.

27. (Currently Amended) ~~A eukaryotic~~The mammalian cell of ~~any of claims 24-26~~claim 26 wherein the cell is a human cell.

28. (Currently Amended) ~~A~~The cell of claim 27 wherein the cell further comprises ~~HIV~~-nucleic acid from HIV.

29. (Currently Amended) ~~A~~The cell of ~~any of claims~~claim 24-27 wherein the cell is ~~a~~-neoplastic cell.

30. (Currently Amended) A vector comprising the DNA molecule of claim 21, or a DNA from which encoding at least one of the RNA molecules~~molecule~~ of ~~any of claims 1-20~~claim 12 can be transcribed.

31. (Currently Amended) ~~A~~The vector of claim 30 comprising the DNA of ~~any of claims 21-23~~claim 21.

32. (Currently Amended) ~~A~~The vector of claim 30 ~~or 31~~ wherein the vector is a plasmid, an ~~adenovirus~~adenoviral vector, an adenoassociated ~~virus~~viral vector, or a ~~retrovirus~~retroviral vector.

33. (Currently Amended) ~~A~~The vector of claim 32 wherein the plasmid is an episomal plasmid.

34. (Currently Amended) A method for inhibiting ~~protein~~-expression of a protein in a eukaryotic cell comprising the step of introducing the RNA of ~~any of claims 1-20~~claim 12, the DNA ~~molecules~~molecule of ~~claims~~claim 21, 23 or the ~~vectors~~vector of ~~claims~~claim 30-32 into the cell.

35. (Currently Amended) ~~A~~The method of claim 34 wherein the eukaryotic cell is a mammalian cell.

36. (Currently Amended) ~~A~~The method of claim 35 wherein the cell is a human cell, a somatic cell, an undifferentiated cell, a dedifferentiated cell, a neoplastic cell, or a chimeric cell.

37. (Currently Amended) ~~A~~The method of claim 34 wherein the RNA, DNA, or vector is introduced into the cell using a vesicle or is ~~delivered~~delivery by microinjection.

38. (Currently Amended) ~~A~~The method of claim 34 wherein the mRNA ~~is~~encodes a protein selected from the group consisting of a cancer-related gene product, a rheumatoid arthritis-related gene product, and a viral gene product.

39. (Currently Amended) ~~A~~The method of claim 38 wherein the mRNA is transcribed from an HIV-derived gene.

40. (Currently Amended) ~~A~~The method of claim 39 wherein the gene ~~is~~selected ~~is~~selected from the group consisting of tat, nef, rev, ma, ca, nc, pg vpu, pr, vif, su, tm, vpr, rt and in.

41. (Currently Amended) A method of inhibiting protein expression from a gene in a cell comprising the step of[;]:

introducing into the cell a linear RNA molecule capable of forming a double-stranded RNA ~~dsRNA complex into a cell~~, wherein the RNA molecule comprises:

(a) a first portion that hybridizes to at least part of a mRNA molecule ~~encoded~~ bytranscribed from a the gene; and

(b) a second portion wherein at least part of the second portion is capable of hybridizing to the first portion.

42. (Currently Amended) ~~A~~The method of claim 41 wherein the second portion comprises a polyadenylation signal positioned at the 3' end of the linear RNA molecule.

43. (Currently Amended) ~~A~~The method of claim 42 wherein the second portion further comprises a ribozyme positioned between the part ~~of the second portion~~ capable of hybridizing to the first portion, and the polyadenylation signal, wherein the ribozyme is capable of removing the polyadenylation signal.

44. (Currently Amended) ~~A~~The method of claim 43 wherein the ribozyme is a cis-acting hammerhead ribozyme.

45. (Currently Amended) ~~A~~The method of claim 41 wherein the cell is a mammalian cell.

46. (Currently Amended) ~~A~~The method of claim 41 wherein the cell is *in vitro*.

47. (Currently Amended) ~~A~~The method of claim 41 wherein the cell is *in vivo*.

48. (Currently Amended) ~~A~~The method of claim 41 wherein the introducing step employs microinjection.

49. (Currently Amended) ~~A~~The method of claim 41 wherein the RNA is ~~eneeded~~ by introduced indirectly by introducing a DNA molecule and the DNA molecule is subsequently transcribed in the cell.

50. (Currently Amended) ~~A~~The method of claim 41 wherein the RNA is introduced ~~as~~with a vector.

51. (Currently Amended) ~~A~~The method of claim 50 wherein the vector is RNA or DNA.

52. (Currently Amended) ~~A~~The method of claim 51 wherein the vector is a plasmid, ~~adenovirus~~adenoviral vector, an adenoassociated ~~virus~~viral vector, or a ~~retrovirus~~retroviral vector.

53. (Currently Amended) ~~A~~The method of claim 41 wherein the RNA is synthesized outside the cell.

54. (Currently Amended) ~~A~~The method of claim 41 wherein the RNA is synthesized inside the cell.

55. (Currently Amended) ~~A~~The method of claim 43 wherein the RNA is retained in the nucleus.

56. (Currently Amended) A method for ~~localizing~~retaining a double stranded RNA~~dsRNA~~ molecule ~~to~~in the nucleus of a cell comprising the step of:

introducing a DNA molecule encoding a linear RNA molecule capable of forming a double stranded RNA~~dsRNA~~ complex into a cell wherein the RNA molecule ~~encoded~~bytranscribed from the DNA molecule comprises:

(a) a first portion that hybridizes to at least a portion of a mRNA molecule ~~encoded bytranscribed from~~ a gene; and

(b) a second portion wherein at least part of the second portion is capable of hybridizing to the first portion and wherein the second portion comprises a polyadenylation signal and a ribozyme positioned between the part of the second portion capable of hybridizing to the first portion and the polyadenylation signal,

wherein the ribozyme is capable of removing the polyadenylation signal thereby retaining the RNA in the nucleus.

57. (Original) The method of claim 56 wherein the ribozyme is a cis-acting hammerhead ribozyme.

58. (Currently Amended) A method for modulating expression of a nucleic acid sequence in a cell comprising exposing the cell to culture medium ~~in which~~ has been used to maintain cells in culture; wherein the cells so maintained ~~comprising~~contain a double stranded RNA~~dsRNA~~ complex comprising a first portion that hybridizes to at least part of a mRNA molecule ~~encoded bytranscribed from~~ a gene; and a second portion wherein at least part of the second portion is capable of hybridizing to the first portion ~~have been maintained in cell culture~~.



59. (Currently Amended) A method of identifying the function of a gene in a cell comprising the ~~steps~~steps of[;]:

(a) ~~binding~~presenting a double stranded RNA~~dsRNA~~ molecule to an ~~mRNA~~ molecule in a cell, wherein the double stranded~~ds~~ RNA molecule comprises a first ~~ribonucleic acid molecule~~portion capable of hybridizing under physiological conditions to at least a portion of an mRNA molecule transcribed from the gene; and a second ~~ribonucleic acid molecule~~portion wherein at least a ~~portion~~part of the second ~~ribonucleic acid molecule~~portion is capable of hybridizing under physiological conditions to the first portion; and

(b) detecting a change in the cell resulting from the ~~binding~~presence of the double-stranded RNA molecule.

60. (Currently Amended) A method of forming a double-stranded RNA in a cell comprising the step of introducing the RNA molecule of ~~any of claims 1-20~~ claim 12 or the DNA molecule of ~~claims 21-23~~ claim 21 into a cell.

61. (Currently Amended) A composition for inhibiting the expression of a gene in a eukaryotic cell comprising:

~~an~~ RNA molecule of ~~claims 1 or 4~~ claim 12 wherein the ~~RNA molecule further comprises an additional RNA~~third portion of ~~ribonucleic acid that~~ enhances the ability of ~~dsRNA~~double stranded RNA to alter transcription from the gene ~~encoding from which the~~ mRNA molecule is transcribed.

62. (Currently Amended) The composition of claim 61 ~~further comprising a third portion of ribonucleic acid interposed between the first and second portions~~ wherein the third portion promotes hybridization between the first and second portion.

63. (Currently Amended) ~~Use of any of the RNA of claims 1-20, the DNA of claims 21-23 or the vectors of claims 31-33 to~~ A method of inhibit inhibiting expression of a gene in a cell comprising the step of introducing into the cell the RNA of claim 12, the DNA of claim 21, or the vector of claim 30.

64. (Currently Amended) A pharmaceutical composition comprising the RNA of ~~claims 1-20~~claim 12, the DNA of ~~claims 21-23~~claim 21, or the ~~vectors~~vector of ~~claims 31-33~~claim 30.

65. (Currently Amended) A microinjection apparatus comprising a pharmaceutical composition comprising the RNA of ~~claims 1-20~~claim 12, the DNA of ~~claims 21-23~~claim 21, or the ~~vectors~~vector of ~~claims 31-33~~claim 30.

66. (Currently Amended) A lipid vesicle comprising the RNA of ~~claims 1-20~~claim 12, the DNA of ~~claims 21-23~~claim 21, or the ~~vectors~~vector of ~~claims 31-33~~claim 30.

67. (Currently Amended) ~~Use of any~~ A method for determining the function of genomic nucleic acid or viral nucleic acid in a cell of the RNA of ~~claims 1-20~~claim 12, the DNA of ~~claims 21-23~~claim 21, or the ~~vectors~~vector of ~~claims 31-33~~claim 30 ~~to determine the function of genomic nucleic acid or viral nucleic acid in a cell comprising:~~

(a) introducing the RNA of claim 12, the DNA of claim 21, or the vector of claim 30 into a cell so as to produce in the cell a double stranded RNA molecule comprising a first portion capable of hybridizing under physiological conditions to at least a portion of an mRNA molecule; and a second portion wherein at least a part of the second portion is capable of hybridizing under physiological conditions to the first portion; and

(b) detecting a change in the cell resulting from the binding.

68. (Newly Presented) A DNA molecule from which the RNA-molecule of claim 4 can be transcribed.

69. (Newly Presented) A DNA molecule from which the RNA-molecule of claim 19 can be transcribed.